Evaluation of the Effects of Multiple Vaccinations Administered in a Stressful Environment on Immunologic Function

NSTC Accessions Training Research and Best Practices Symposium: From Civilian to Warrior 23-25 Aug 2005

CDR Margaret Ryan, MC, USN
CDR Kevin Russell, MC, USN

DoD Center for Deployment Health Research
Naval Health Research Center, San Diego

The DoD Center for Deployment Health Research

Commissioned in 1998.
Now the largest team of epidemiologic
researchers in DoD.

Research is competitively funded
by DoD, NIH, and others.

32 active protocols in FY05,
many focused on studies of respiratory infections
and vaccines.

The DoD Center for Deployment Health Research and NSTC Great Lakes

Collaborating on respiratory infection and vaccine projects since Aug 1995.

Highlights include:

- Surveillance for viral pathogens (including adenovirus) causing febrile respiratory illness
- Surveillance for Group A strep, typing and antibiotic resistance
- Surveillance for invasive pneumococcal illness
- Clinical trial of 23-valent pneumococcal vaccine (complete)
- Clinical trial of re-developed adenovirus vaccines (upcoming)

e DoD Center for Deployment Health Research: Other Respiratory Infection Projects

- DoD-wide population-based, laboratory-supported surveillance of infections among all services
- Shipboard surveillance and outbreak investiga
- Deployment surveillance and FDPMU s
- Development of advanced lab capabili and molecular studies

HRC Respiratory Disease Surveillance Sites

DoD Center for Deployment Health Research: Vaccine Studies

- Knowledge, attitudes, and beliefs about vaccines
- Smallpox vaccine and health outcomes
- Smallpox vaccine and reproductive health
- National Smallpox Vaccine in Pregnancy Registry
- Smallpox vaccine – case-control study of myopericarditis
- Smallpox vaccine-induced immunity (Mayo Clinic)
- Anthrax vaccine and health outcomes
- Anthrax vaccine and birth defects
- Clinical trial of pneumococcal vaccine
- Clinical trial of adenovirus vaccine
- Multiple simultaneous vaccines and immune response

The Immunologic Effects of Multiple Simultaneous Vaccinations

Background

- Multiple simultaneous vaccinations (MSV) historically considered safe by CDC and others. Limited data, however, are available.
- Studies suggest MSV in a stressful environment could lead to multi-symptom illness.[1]
- Of military and clinical importance:
  - ✓ Recruit training centers
  - ✓ Deployments
  - ✓ Travel clinics
  - ✓ Pediatric clinics

** Every patient encounter should be optimized **

[1]Rook GAW, Zumla A. GW Syndrome: due to a shift in cytokine balance towards a Th2 profile? Lancet 1997;349:1831-3.

The Immunologic Effects of Multiple Simultaneous Vaccinations

Current recruit vaccines protect against:

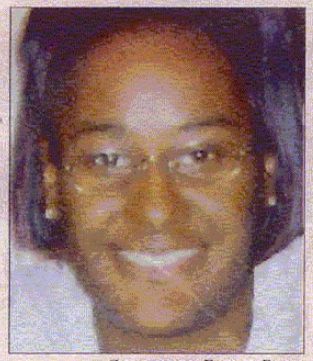
- measles, mumps, rubella, varicella, influenza, hepatitis A, hepatitis B, polio, diphtheria, tetanus, meningococcus, Yellow Fever

Future additions to the vaccine schedule may include:

- adenovirus, pertussis (will be added when available)
- smallpox, anthrax, pneumococcus, plague, typhoid, JEV (available, not on recruit schedule at this time)
- HPV, HSV, Group A strep, RSV (not yet available, but under development and of potential value to

US Army Times
December 6, 2004

COURTESY OF MOSES LACY



COURTESY OF BAWANA PERRY

Left, Army Spc. Rachel Lacy, 22, died 33 days after she received multiple vaccinations required for duty in the Persian Gulf region. Army Reserve Pfc. Arwana Lattimore-Oliver, 28, became severely ill after getting multiple vaccinations and also died.

Too many vaccines, too quickly?

Stories by Deborah Funk
TIMES STAFF WRITER

Army Spc. Tyran Duncan no longer needs a machine to draw breath, but his hands can't grip tightly and he wears braces on his legs to help him walk.

Duncan, 20, who was temporarily medically retired Nov. 24, hasn't completely recovered from the Guillain-Barré syndrome that struck him two years ago, a few weeks after he received numerous military-related vaccinations.

But at least he's not completely paralyzed anymore.

He believes the vaccinations caused his health problems, but since he received multiple shots

American troops have been given vaccines to protect them against diseases their leaders say threaten their health and the military's readiness.

In the Revolutionary War, troops were inoculated with live smallpox. After the Spanish-American War, typhoid vaccine was introduced. By World War II, U.S. troops got multiple jabs, often at the same time, a practice that continues today.

Medical experts say numerous simultaneous shots generally are safe, and studies in young children who get multiple shots have not proved otherwise.

"You are bombarded with far more ... immunologic challenges in your environment than you'd ever

The Immunologic Effects of Multiple Simultaneous Vaccinations

Hypothesis

- MSV in a stressful environment result in a Th2 shift of the immune system and potential for adverse reactions and multi-symptom illness.

Objectives

- Determine if MSV in a stressful environment induce Th2 shift.
- Determine if MSV in a stressful environment are associated with adverse health events, as compared to staggered administration of vaccines.

The Immunologic Effects of Multiple Simultaneous Vaccinations

Methods

- Enroll 650 Naval Recruits randomized to 2 groups
  - ✓ Current Schedule (325)
  - ✓ Staggered Schedule (325)
- Blood sample (10cc) taken on day 1, 30, and 45
- Questionnaire day 1 and 45 (near end of training)

Laboratory Testing

- Cortisol levels (~indicative of stress)
- Th1 associated cytokines: IL-2; IL-12, TNF-α, TNF-γ, IFN-γ
- Th2 associated cytokines: IL-4, IL-5, IL-6, IL-10, IL-13

The Immunologic Effects of Multiple Simultaneous Vaccinations

Challenges

- Recruit training environment has no room for “extra” work
- No vaccines may be eliminated and several cannot be ‘staggered’ (e.g., MMR, varicella, meningococcal, influenza must be given at entrance)

Addressing challenges

- NHRC is working closely with Great Lakes professionals to ensure no/minimal disruption in work.
- NHRC is hiring staff to support on-site work and augment Great Lakes team.
- Project should be limited to 3 months on-site work.

The Immunologic Effects of Multiple Simultaneous Vaccinations

Value

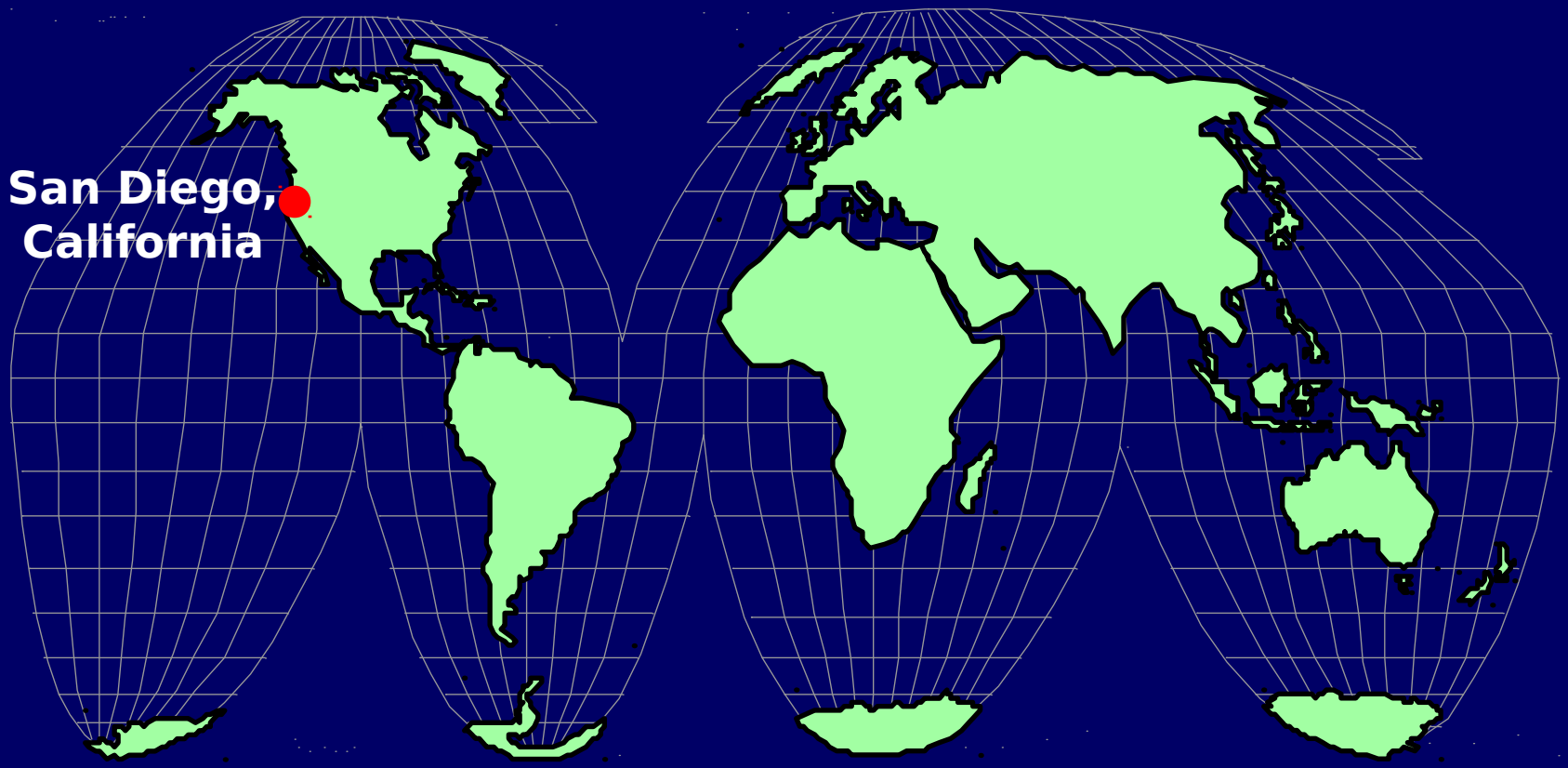
- Monitoring of adverse events may reveal new information on as-yet-unrecognized symptom groupings, or rare but established adverse events, such as Guillain-Barré Syndrome.
- The project is of great interest to military and civilian public health professionals, in the US, UK, and other countries.
- Work may reaffirm the safety of multiple vaccinations in our military populations.

The Immunologic Effects of Multiple Simultaneous Vaccinations

Funding and Endorsement

- Funded by US Army Medical Research Acquisition Activity (USAMRAA) under the competitive Peer-Reviewed Medical Research Program.
- Endorsed by the Armed Forces Epidemiology Board.
- Approved by HSRRB and NHRC IRB (BUMED).
- UK collaborators (Dr. Simon Wessely and Dr. Mark Peakman) closely engaged.

DoD Center for Deployment Health Research



http://www.nhrc.navy.mil/rsch/code25/program5.htm

Notes from past briefs

21 March 2005
RDM Jones, COMMANDER, NSTC/Navy Region MIDWEST
CAPT Anderson, Commanding Officer, NHGL
CAPT Moran, Commanding Officer, RTR-GL

25 March 2005
DoD-VA Joint Research Symposium, North Chicago VAMC

July 2005
NSTC, VA Blood Bank, Scheduling, Medical Records, Credentialing, Legal (MOUs), USS Red Rover (LCDR Andre), USS Tranquility